ehp Environmental Health PERSPECTIVES
ehponline.org
Published by the National Institute of Environmental Health Sciences

Serum Dioxin Concentrations and Age at Menopause

Brenda Eskenazi, Marcella Warner, Amy R. Marks, Steven Samuels, Pier Mario Gerthoux, Paolo Vercellini, David L. Olive, Larry Needham, Donald G. Patterson, Jr., and Paolo Mocarelli

doi:10.1289/ehp.7820 (available at http://dx.doi.org/)
Online 24 March 2005

The National Institute of Environmental Health Sciences
National Institutes of Health
U.S. Department of Health and Human Services

Serum Dioxin Concentrations and Age at Menopause

Brenda Eskenazi[1*], Marcella Warner[1], Amy R. Marks[1], Steven Samuels[1,2], Pier Mario Gerthoux[3], Paolo Vercellini[4], David L. Olive[5], Larry Needham[6], Donald G. Patterson, Jr.[6], Paolo Mocarelli[3]

[1]School of Public Health, University of California at Berkeley, Berkeley, CA

[2]School of Public Health, State University of New York, Albany, NY

[3]Department of Laboratory Medicine, University of Milano-Bicocca, School of Medicine, Hospital of Desio, Desio-Milano, Italy

[4]Department of Obstetrics and Gynecology, Mangiagalli Hospital, University of Milan, Milan, Italy

[5]Department of Obstetrics and Gynecology, University of Wisconsin Medical School, Madison, WI

[6]Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA

*Address reprint requests to Brenda Eskenazi, Ph.D., School of Public Health, University of California, 140 Warren Hall, Berkeley, CA 94720-7360,

Phone: 510-642-3496 Fax: 510-642-9083 Email: eskenazi@berkeley.edu

Running title: Serum dioxin and age at menopause

Key words: dioxin, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, TCDD, endocrine disruptors, menopause, Seveso, Cox proportional hazards

Acknowledgements: We thank Stefania Casalini for coordinating data collection at Hospital of Desio and Wayman Turner from the Centers for Disease Control and Prevention for serum TCDD measurements. This work was supported by the following grants: R01 ES07171 and F06 TW02075-01 from the National Institutes of Health, R82471 from the U.S. Environmental Protection Agency, EA-M1977 from the Endometriosis Association, 2P30-ESO01896-17 from the National Institute of Environmental Health Sciences, and #2896 from Regione Lombardia and Fondazione Lombardia Ambiente, Milan, Italy. A conflict of interest was not reported.

Abreviations

BMI	body mass index
CI	confidence interval
DDE	dichlorodiphenyldichloroethene
FSH	follicle stimulating hormone
HR	hazard ratio
IQR	interquartile range
LH	luteinizing hormone
OC	oral contraceptive
PBB	polybrominated biphenyl
PCB	polychlorinated biphenyl
PCDD	polychlorinated dibenzo-*p*-dioxin
PCDF	polychlorinated dibenzofuran
ppt	parts per trillion
SWHS	Seveso Women's Health Study
SD	standard deviation
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
TEQ	dioxin toxic equivalents

OUTLINE OF SECTON HEADERS

Abstract
Introduction
Materials and Methods
    Study population
    Procedure
    Serum TCDD Laboratory Analyses
    Definition of Menopause
    Statistical Analyses
Results
Discussion
References

ABSTRACT

2,3,7,8-Tetrachlorobenzo-*p*-dioxin (TCDD), a halogenated compound that binds the aryl hydrocarbon receptor, is a byproduct of numerous industrial processes including waste incineration. Studies in rats and monkeys suggest that TCDD may affect ovarian function. We examined the relationship of TCDD and age at menopause in a population of women residing near Seveso, Italy in 1976, at the time of a chemical plant explosion. We included 616 of the women who participated 20 years later in the Seveso Women's Health Study. All women were premenopausal at the time of the explosion, had TCDD levels measured in serum collected soon after the explosion, and were ≥35 years old at interview. Using proportional hazards modeling, we found a 6% non-significant increase in risk of early menopause with a 10-fold increase in serum TCDD. When TCDD levels were categorized, compared to women in the lowest quintile (<20.4 ppt), women in quintile II (20.4 - 34.2 ppt) had a hazard ratio (HR) of 1.1 (p = 0.77); quintile III (34.3 - 54.1 ppt) had a HR of 1.4 (p = 0.14); quintile IV (54.2 - 118 ppt) had a HR of 1.6 (p = 0.10); and quintile V (>118 ppt) had a HR of 1.1 (p = 0.82) for risk of earlier menopause. The trend toward earlier menopause across the first four quintiles is statistically significant (p=0.04). These results suggest a non-monotonic dose-related association with increasing risk of earlier menopause up to about 100 ppt TCDD, but not above.